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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/464,795

12/16/1999

NING ZHANG

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8087

7590

04/28/2006

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EXAMINER

FALK, ANNE MARIE

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 04/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

09/464,795

Applicant(s)

ZHANG ET AL.

Examiner

Anne-Marie Falk, Ph.D.

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 31 March 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).


4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 38, 40, 41, 45, 46, 49, and 65-68.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.


ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Anne-Marie Falk, Ph.D.
Primary Examiner
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Continuation Sheet (PTOL-303)

Continuation of 5. Applicant's reply has overcome the following rejection(s): the rejection of Claims 38, 40, 41, 45, 46, 49, and 65-68 under 35 U.S.C. 112, second paragraph.

Continuation of 11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:

With regard to the utility rejection, Applicants assert, at pages 5-6 of the response, that the Examiner acknowledges there is a well-established utility set forth in the specification. On the contrary, the Examiner alerted Applicant that the utility they were referring to was actually an **asserted** utility. See the Office Action of 2/8/06 at page 6, paragraph 1. An asserted utility should not be confused with a well-established utility. Applicants further assert that a utility rejection cannot be based on an allegation that the claims are somehow "overly broad" and that they are not required to limit their claims to promoters that recapitulate native gene expression in order to show utility. On the contrary, since it is the specification itself that **asserts** that the utility of the claimed invention is to provide transgenic mice comprising constructs that function to recapitulate native gene expression, it cannot be said that claims directed to the use of promoters in artificial contexts satisfy this **asserted utility**. An asserted utility must be specific to the claimed subject matter. The specification is clear that the intention is to create a construct and experimental system that recapitulates **native gene expression**, not gene expression in an artificial context. The specification does not provide specific guidance for creating constructs, within the scope of the claims, that have this utility.

With regard to the written description rejection, Applicants argue, at pages 6-7 of the response, that nucleotide sequences need not be described because the constructs are assembled from known sequences. As noted in the prior Office Action, mailed 2/8/06, at page 6, the rejection of record does not pertain to nucleotide sequences. Thus, the argument that nucleotide sequences of stress-inducible

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Continuation Sheet (PTOL-303)

promoters and sequences encoding light generating proteins were well known at the time of filing is not persuasive. The rejection of record is grounded in the failure of the specification to describe those constructs that will provide for native gene expression and thereby be representative of **native gene expression**, such that the effect of an analyte on the construct will be representative of the effect of the analyte on the promoter (and its elements) in its native context. The specification makes it clear that the desired goal of the invention is to prepare constructs **relevant to native gene expression** in an *in vivo* context and then to use those constructs to observe the effects of various treatments or agents on the promoter activity, but the specification has not described those constructs that will provide for **native gene expression**.

With regard to the enablement rejection, Applicants assert, at pages 7-8 of the response, that the specification teaches one of skill in the art how to make animals including two or more constructs and that the Office has not provided any reason to doubt that transgenic mice comprising multiple constructs could be made. As explained in the prior Office Actions, and particularly at page 7 of the Office Action mailed 5/17/05, the existence of transgenic mice expressing light generating proteins is not sufficient to enable the claimed invention because the **claimed** invention requires the generation of transgenic mice having promoters that regulate expression of the light generating proteins in a manner that is **predictive** of native gene expression (the only asserted utility for the claimed transgenic mouse). The particular promoter portions (and upstream portions of the regulatory region of the gene) used and the method of inserting the expression cassettes into the genome of the mouse are critical to the operability of the claimed invention. The specification teaches that only those promoter portions that recapitulate native gene expression have utility in the claimed invention, but the specification fails to enable the identification of such promoter portions such that the native context is retained when the promoter is truncated and inserted into an expression cassette, which is then inserted into the genome of a mouse (in a new genetic context).

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Continuation Sheet (PTOL-303)

Therefore, the rejections under 35 U.S.C. 101 and 112, first paragraph, are maintained for reasons of record.